# REPROCELL

## The REPROCELL Group provides products and services across the entire drug discovery process



**REPROCELL's human tissue technology predicts clinical success by using the closest possible model of drug behavior in humans.**

REPROCELL offers contract laboratory services to pharmaceutical and biotechnology companies, providing data on the likely effects of drug candidates before they are given to human volunteers and patients.

By understanding the safety and effectiveness of a drug in a pharmaceutical lab test, much more expensive clinical trials can be de-risked.

**reprocell.com**

# 1. TARGET IDENTIFICATION

**Determine the biological origin of the disease and potential targets for intervention using human tissue samples. Investigate receptor sites on particular cells that may be abberantly expressed in the disease state.**

## The BioServe Global Human BioRepository

REPROCELL's BioServe Global BioRepository is one of the largest commercial human tissue banks in the world.

All samples are linked to approximately 200 data points about demographic, phenotypic, pathology and diagnostic information and drug history.

| **We have it...** | **Our network has it...** | **Or, we can collect it** |
|---|---|---|
| Our BioRepository contains more than 600,000 human serum, frozen tissue, DNA, RNA, FFPE and other samples collected from over 120,000 consented and anonymized patients on four continents. | The BioServe Biospecimen Repository Network of partner organizations also provides broader access to rare samples and the ability to source material specific to your research needs through prospective collections. | BioServe continues to establish procurement partnerships with speciality clinics around the USA in a number of indications/ diseases, including autoimmune, inflammatory and rheumatology, urology and oncology. |

## 3. LEAD IDEN...

**Perform high throughput screening of drug ... in 3D for physiologically meaningful data to ...**

## Alvetex 3D Cell Culture Models

3D cell cultures using REPROCELL's Alvetex technology deliver more *in vivo*-like results than traditional 2D monolayer cultures.

- Highly porous inert scaffold made from cross-linked polystyrene (200 µm thick).
- Suitable for a wide range of cell types including primary or iPSC-derived cells from most organs, various stem cells, cancer, and complex co-culture models.
- Automation – 96 well and 384 well plate formats compatible with high throughput screening and a variety of assays and techniques.
- Build more predictive biological models by maintaining *in vivo* physiological properties, enhancing cell viability and longevity.
- Simple histology, imaging and RNA/ protein isolation analysis endpoints.
- Add perfusion in 3D for another step closer to *in vivo*.

---

**TARGET IDENTIFICATION** › **TARGET VALIDATION** › **LEAD IDENTIFICATION** ›

---

# 2. TARGET VALIDATION

**Investigate the target's potential as a drug using fresh patient tissue or patient-specific iPSC-derived disease model cells.**

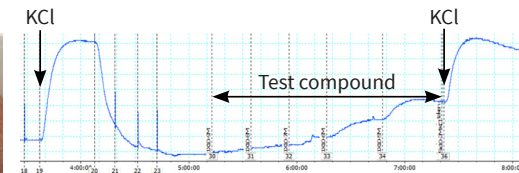## Assess the Efficacy of Your Drug Candidate in Diseased and Healthy Tissue

- Compare activation of potential target and functional response.
- Explore differences in drug response between patients and relate responses to clinical histories.

KCl        KCl

Test compound
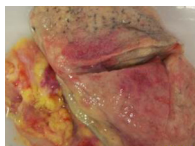
COPD lung          Healthy lung          Measure bronchoconstriction or dilation

## REPROCELL iPSC-derived Differentiated Cells

REPROCELL offers iPSC-derived differentiated cardiac cells, hepatocytes, and neurons suitable for use in basic research as model systems for a variety of applications. Unlike primary cells which may come from random donors with variable genetic backgrounds, these iPSC-derived cells have strong lot-to-lot performance consistency.

REPROCELL also has the ability to prepare customized versions of iPSC-derived cell types as required.

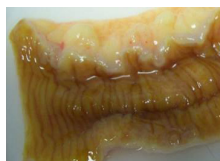**ReproCardio2™**          **ReproNeuro™**          **ReproHepato™**

## 4. LEAD OPT...

**Accurately predict *in vivo* bioavailability and ... eliminating well known differences between ...**

## Determine the Potency of Your Drug

Small intestine ile...

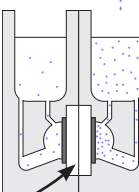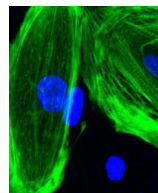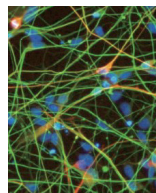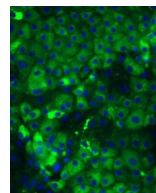- Compare the potency of your candidate drug versus other drugs on the market.

## Increase the Confidence of Your First-in-...

- Measure compound permeability, transporter, or ... tissue in order to accurately predict *in vivo* bioava...
- Eliminate well-known differences between human ... metabolism by using human tissue.

Healthy fresh small intestine          Ussing chambers

candidates on complex cell systems grown
identify potential leads.
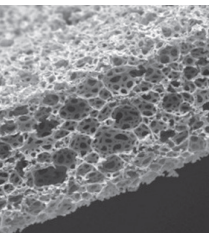


**alvetex**

SEM of Alvetex Scaffold
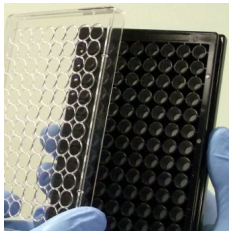
96 well and 384 well plate formats available

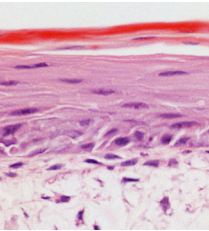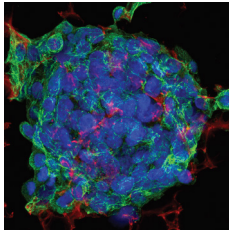Co-culture of primary keratinocytes and primary dermal fibroblasts forming a full-thickness human skin construct

Triple fluorescent staining of HepG2 cells grown in 3D on Alvetex Scaffold

# 5. PRE-CLINICAL SAFETY

**Are your test compounds safe in humans? Evaluate the pre-clinical safety of compounds using human tissue.**

## Find Out if Your Drug is Safe in Human Tissue Prior to Clinical Trials
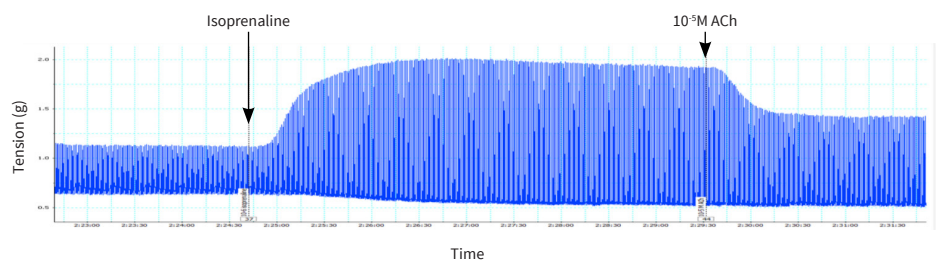
**biopta**

- Measure adverse effects on heart or lung muscle contractility or blood vessel contraction/dilation.
- Conduct comparative studies across species.

Human heart

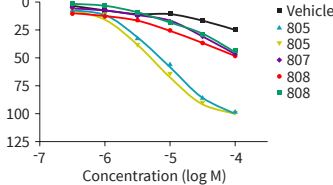Force of contraction measured in organ baths



Isoprenaline          $10^{-5}$M ACh

Tension (g)

Time

---

**LEAD OPTIMIZATION** ⟩ **PRE-CLINICAL SAFETY** ⟩ **CLINICAL TRIALS**

---

TIMIZATION

drug metabolism using human tissue,
human and alternative model systems.

**biopta**

**Effect of Inhibitors of Chloride Secretion in Human Ileum**
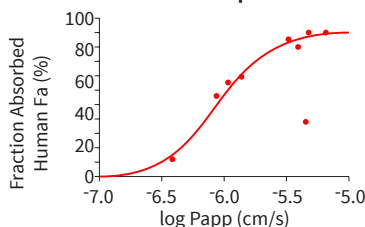
■ Vehicle
▲ 805
▼ 805
♦ 807
● 808
■ 808

Concentration (log M)

Man Dose Estimate

metabolic enzyme activity in human intestinal
ailability and drug metabolism.

and animal or cell models in bioavailability and

*In vitro* human gut permeability correlates well to expected clinical absorption
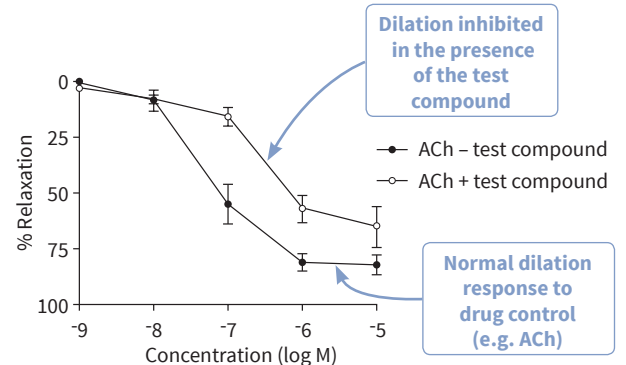
Fraction Absorbed Human Fa (%)

log Papp (cm/s)

# 6. CLINICAL TRIALS

**Troubleshoot clinical problems by investigating the mechanisms of clinically-observed adverse effects using human fresh tissues.**

## Investigate Unexpected Side Effects Observed in Clinical Trials

**biopta**

- Obtain independent verification of your clinical results.
- Examine adverse effects e.g. unforeseen effects on blood vessel dilation/constriction effecting blood pressure.

Human small artery

**Constriction**

**Dilation**

**Dilation inhibited in the presence of the test compound**

● ACh – test compound
○ ACh + test compound

**Normal dilation response to drug control (e.g. ACh)**

% Relaxation

Concentration (log M)
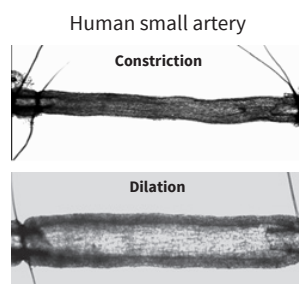
REPROCELL generates high quality translational data to help you make informed decisions during drug development.
Only a selection of our available tissues and assays is shown.

See our website or contact us for more information.

## Why REPROCELL?

Clinical trials for Investigational New Drugs (IND) are perhaps the biggest cost associated with drug development. And yet, up to 90% of all INDs fail at some phase in clinical trials. This is mainly attributable to the fact that most IND research and development is done in animal models and cell culture. The translation of efficacy, clinical safety and toxicology data to humans is not assured.

The REPROCELL Group has ready access to live human tissues through our extensive clinical networks, in addition to human iPSC-derived 3D cell model systems to create custom assays that can provide predictive human data to de-risk your drug discovery programs. No other company has this unique combination of expertise and capabilities.

## REPROCELL Brands



The leading provider of stem cell science and differentiation reagents: we provided media for the creation of the first iPSCs



The world's largest commercial biorepository with more than 600,000 samples



The most efficient process for creation of clinically relevant iPSCs, without the use of vectors
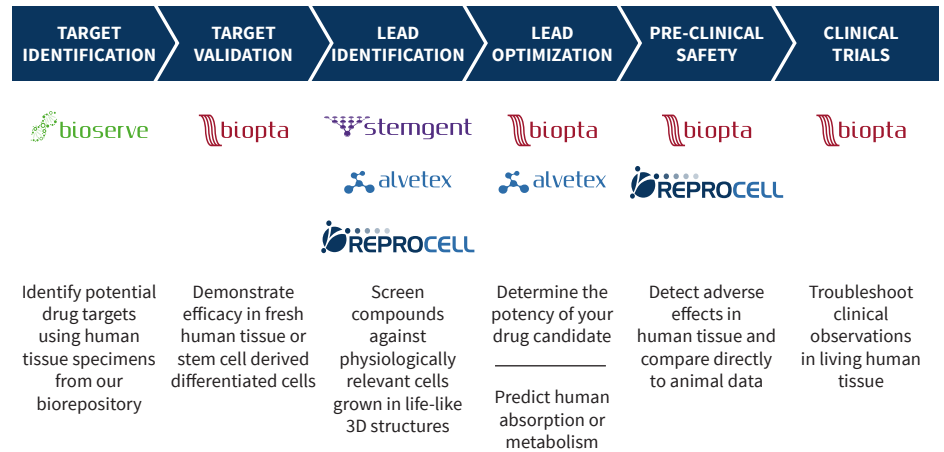


Award-winning technology for creation of 3D human tissues *in vitro*



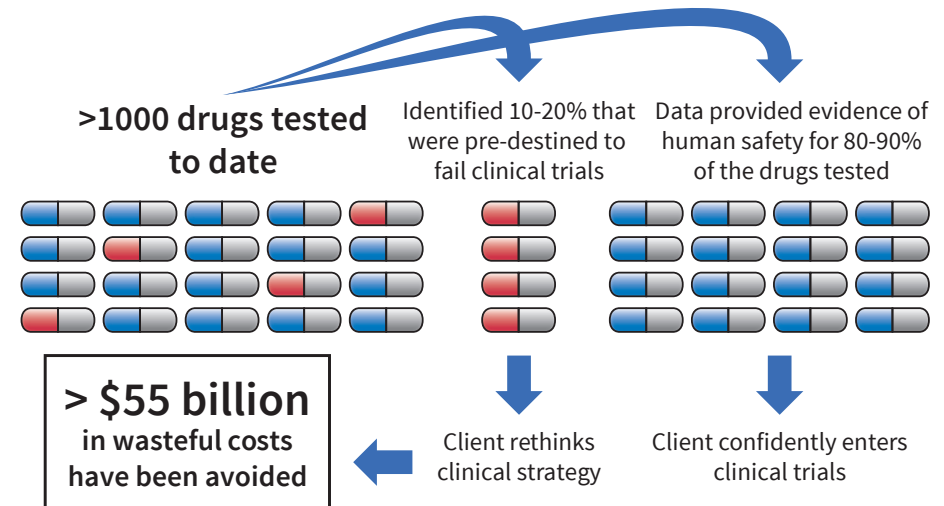The only CRO offering predictive assays in human fresh tissues

## The REPROCELL Group provides products and services across the entire drug discovery process

| TARGET IDENTIFICATION | TARGET VALIDATION | LEAD IDENTIFICATION | LEAD OPTIMIZATION | PRE-CLINICAL SAFETY | CLINICAL TRIALS |
|---|---|---|---|---|---|
| bioserve | biopta | stemgent / alvetex / REPROCELL | biopta / alvetex | biopta / REPROCELL | biopta |
| Identify potential drug targets using human tissue specimens from our biorepository | Demonstrate efficacy in fresh human tissue or stem cell derived differentiated cells | Screen compounds against physiologically relevant cells grown in life-like 3D structures | Determine the potency of your drug candidate ———— Predict human absorption or metabolism | Detect adverse effects in human tissue and compare directly to animal data | Troubleshoot clinical observations in living human tissue |

**De-risking the drug discovery process by use of *in vitro* human data**

## Nous aidons nos clients à gérer leur risques et à reduire leur dépenses budgétaires

Démontrer l'efficacité et la non-dangerosité dans un modèle humain à un stage précoce du développement pharmaceutique confère une valeur commerciale énorme aux programmes de recherche de nos clients. Pour 10 à 20% des médicaments que nous avons testés, le client a décidé de re-penser une stratégie clinique qui semblait destinée à échouer d'aprés les résultats des analyses sur tissus humains. Nous estimons que ceci a resulté à des économies nettes de plus de 55 milliards de dollars pour le budget de nos clients.

**>1000 drugs tested to date**

**Identified 10-20% that were pre-destined to fail clinical trials**

**Data provided evidence of human safety for 80-90% of the drugs tested**

**> $55 billion in wasteful costs have been avoided**

Client rethinks clinical strategy

Client confidently enters clinical trials